Etsrp/ER71 mediated stem cell differentiation into vascular lineage

Grant Award Details

Etsrp/ER71 mediated stem cell differentiation into vascular lineage

Grant Type: Basic Biology III

Grant Number: RB3-02165

Project Objective: The main objective of this project is to generate endothelial cells from hESCs using gene transfer technology and regulated gene expression.

Investigator:

Name:	Shuo Lin
Institution:	University of California, Los Angeles
Type:	PI

Human Stem Cell Use: Embryonic Stem Cell

Award Value: $1,378,781

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Reporting Period: NCE (Year 4)

View Report

Grant Application Details

Application Title: Etsrp/ER71 mediated stem cell differentiation into vascular lineage

Public Abstract: Human embryonic stem cells (hESC) have the potential to differentiate into all of the cell types that make up the body. Therefore, hESCs are promising tools for the treatment of degenerative diseases and for use in regenerative medicine. One highly desirable use of hESCs is to treat cardiovascular disease. Cardiovascular disease is a leading cause of mortality and morbidity in the state and country. Cardiovascular disease is caused by damage to blood vessels and the ability to repair this damage will improve disease outcomes. However, the ability to efficiently differentiate hESCs down cardiovascular lineages to generate large numbers of cells on a therapeutically relevant scale is lacking. The goal of this project is to develop a protocol for the differentiation of hESCs into vascular endothelial cells for the treatment of cardiovascular disease. Initially we will study the expression of vascular precursor cell genes during embryoid body formation from hESCs. Then, using gene transfer technology and regulatable gene expression of transcription factors that induce the vascular cell lineage, we will "tune" treated hESCs to optimize derivation of endothelial cells. We will then use these cells in a pre-clinical mouse model of ischemic heart damage to test their ability to integrate into the damaged tissue and restore circulatory function. Additionally, we will use these cells to study the molecular mechanisms of endothelial cell differentiation. These studies will increase our knowledge of hESC biology, endothelial cell development, and suggest methods for therapeutic use of hESCs.

Statement of Benefit to California: Cardiovascular disease, including heart disease, heart failure, and stroke, is the number one cause of death in the state of California. Additionally, patients suffering with these conditions have decreased quality of life and represent a significant financial and emotional burden to both their families and the state in general. Novel treatments to block or reverse the progression of cardiovascular disease will benefit the patient physically, the caregiver emotionally, and relieve the financial burden to everybody. Recently, the use of human stem cells has been proposed as a therapeutic treatment for cardiovascular disease. Addition of these cells to injured tissue has the potential to prevent the loss of more tissue and regenerate lost tissue. However, before such treatments become available, the basic biology of these cells must be understood to maximize treatment efficiency and prevent unwanted side effects. We have identified a critical gene in the development of blood vessel precursor cells and propose to use it to optimize the generation of blood vessel cells from human embryonic stem cells. In addition we will carefully examine the molecular events underlying the transition from stem cell to blood vessel precursor. The potential knowledge gained from these studies has implications for controlling blood vessel overgrowth in diseases such as cancer and diabetic retinopathy as well as blood vessel dysfunction in diseases such as cardiovascular disease and peripheral artery disease. These findings will benefit the field of stem cell research and basic developmental biology with future research directions based on these results. In addition to the clinical and scientific applications of these studies, the young scientists being trained in the laboratory will provide the foundation for future research in academia or industry in California. The success of this project will enhance the already stellar reputation of the state of California as a leader in the stem cell field.